REMARKS

Claims 1-13 are pending in the application. The claims have not been amended by the present response.

Allowable Subject Matter

At page 7 of the Office Action, the Examiner stated that claims 3-5 and 11-13 are allowed. In view of the remarks presented herein, applicants respectfully submit that all of the pending claims are in condition for allowance.

Priority

At pages 2-3 of the Office Action, the Examiner stated that the claimed invention is entitled to a priority date of May 7, 1997 (the filing date of application serial number PCT/US97/07726). Applicants agree that the claims are entitled to a priority date of at least May 7, 1997. However, in view of the remarks below establishing that the cited references do not anticipate the claimed invention, examination of this application does not require a determination of whether the claims are also entitled to the priority date of an earlier priority application.

35 U.S.C. §112, First Paragraph (Written Description)

At pages 3-5 of the Office Action, claims 1, 2, and 6-10 were rejected as allegedly containing subject matter that was not described in the specification in such a way that one skilled in the art can reasonably conclude that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action appears to maintain this rejection, at least in part, based upon the assertion that "[a] genus that embraces widely variant species cannot be achieved by disclosing only one species within the genus."

Applicants respectfully traverse the rejection in view of the following remarks.

The present application describes the identification and characterization of the human RetL3 protein (SEQ ID NO:21) and the murine RetL3 protein (SEQ ID NO:17). These two

species of RetL3 are 76.8% identical to each other (see specification at page 37, paragraph 0116). Given that each of the disclosed RetL3 proteins constitutes a functional polypeptide that interacts with the receptor tyrosine kinase Ret, the skilled person would readily expect that at least those amino acids (i.e., 23.2% of the amino acid positions) that diverge between the two RetL3 species are likely to be amenable to change without eliminating biological activity. As compared to this disclosure, claims 1, 2, and 6-10 are directed to polypeptides that encompass variation that is less than that existing between the RetL3 species described in the specification. In particular, independent claim 1 is directed to an isolated polypeptide that (i) comprises an amino acid sequence that is at least 80% identical to the sequence of SEQ ID NO:17 or SEQ ID NO:21, and (ii) interacts with and triggers dimerization or autophosphorylation of the receptor protein Ret. The genus of polypeptides encompassed by claim 1 does not have substantial variation, since all such polypeptides must have a specified activity and contain a sequence that is at least 80% identical to SEQ ID NO:17 or SEQ ID NO:21. The human and murine RetL3 polypeptides disclosed in the specification are representative of the claimed genus because: all polypeptides encompassed by the claimed genus are required to be even more highly related (i.e., at least 80%, 90%, or 95% identical) to SEQ ID NO:17 or SEQ ID NO:21 than the variation (76.8% identity) that exists between the RetL3 species exemplified in the application; and routine assays are well known in the art for identifying variants having the functional activity specified by the claim.

In light of the disclosure contained in the application as filed, the skilled artisan would have concluded that the inventors were in possession (at the time of filing of the present application) of the necessary common attributes possessed by the members of the claimed genus. Accordingly, applicants respectfully submit that independent claim 1 and claims 2 and 6-10 that depend therefrom satisfy the written description requirement. Applicants request that the Examiner withdraw the rejection.

35 U.S.C. §112, First Paragraph (Enablement)

At page 5 of the Office Action, claims 1, 2, and 6-10 were rejected as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention. The Office Action appears to maintain this rejection, at least in part, based upon the assertion that "the claims continue to read on a number of polypeptides because remiss from the specification is sufficient guidance as to what amino acid residues and domains are tolerable to changes and would render polypeptides that would function in the manner that is germane to the implementation of the molecules."

Applicants respectfully traverse the rejection in view of the following remarks.

Independent claim 1 is directed to an isolated polypeptide that (i) comprises an amino acid sequence that is at least 80% identical to the sequence of SEQ ID NO:17 or SEQ ID NO:21, and (ii) interacts with and triggers dimerization or autophosphorylation of the receptor protein Ret.

As noted above in response to the written description rejection, the polypeptides encompassed by claims 1, 2, and 6-10 are required to be even more highly related (i.e., at least 80%, 90%, or 95% identical) to SEQ ID NO:17 or SEQ ID NO:21 than the variation (76.8% identity) that exists between the RetL3 species exemplified in the application. The skilled person would expect at a minimum that at least those amino acids (i.e., 23.2% of the amino acid positions) that diverge between the two RetL3 species disclosed in the application are likely to be amenable to change without eliminating biological activity. In view of the specification's disclosure of the divergent sequences of human and murine RetL3, combined with the knowledge in the art that conservative amino acid substitutions can be made in a protein so as to reduce the likelihood that a given amino acid change will result in a loss of function, it would have required no undue experimentation for the skilled person to prepare a polypeptide that contains an amino acid sequence that is at least 80% (or at least 90% or 95%) identical to SEQ ID NO:17 or SEQ ID NO:21 and that is expected to retain the RetL3 biological activity recited in the claims. Standard mutagenesis techniques can be used produce variants of RetL3

that are at least 80%, 90%, or 95% identical to the RetL3 sequence of SEQ ID NO:17 or SEQ ID NO:21.

In addition to having been able to produce RetL3 sequence variants having at least 80% (or at least 90% or 95%) identity with SEQ ID NO:17 or SEQ ID NO:21, it would have required no undue experimentation for the skilled artisan to identify those variants that retain the ability to interact with and trigger dimerization or autophosphorylation of the receptor protein Ret (i.e., the functional activity recited in the claims). Readily screenable assays can be used to determine whether a given protein possesses this functional activity.

In light of the foregoing remarks, applicants respectfully submit that one of ordinary skill in the art would have been able, at the time of filing of the present application, to make and use the claimed polypeptides without undue experimentation and with a reasonable expectation of success. Accordingly, applicants request that the Examiner withdraw the rejection of independent claim 1 and dependent claims 2 and 6-10.

35 U.S.C. §102(e), First Paragraph (Anticipation)

At pages 6-7 of the Office Action, claims 1, 2, and 6-10 were rejected as allegedly anticipated by each of Fox et al., U.S. Published Application No. 20040235714 ("Fox I") and Fox et al., U.S. Patent No. 7,138,251 ("Fox II").

Applicants respectfully traverse the rejections in view of the following remarks.

The Fox I patent application was filed on June 18, 2004 and is a continuation of application serial number 08/866,354, filed on May 30, 1997, which application gave rise to the Fox II patent. Because Fox I is a continuation of Fox II, the two references are expected to have identical specifications. Consistent with this expectation, the two anticipation rejections contain nearly identical language and assert that sequences in Fox I and Fox II designated numbers 42 and 38 "share at least 92% and 99% sequence homology with Applicants' SEQ ID NO: 17 and 21, respectively."

As noted above in the section entitled "Priority," the Office Action asserts that the pending claims of the present application are entitled to a priority date of May 7, 1997. However, Fox I and Fox II were both filed *after* May 7, 1997 (i.e., on June 18, 2004 and May 30, 1997, respectively). Fox I and Fox II both claim priority to the following three prior patent applications: (i) application serial number 08/837,199, filed on April 14, 1997; (iii) application serial number 60/017,221, filed on May 9, 1996; and (iii) application serial number 60/015,907, filed on April 22, 1996. SEQ ID NOS:42 and 38 of Fox I and Fox II correspond, respectively, to proteins termed "rat GRR3" and "human GRR3." Fox I and Fox II describe the cloning and expression of GRR3 in Example 11 and disclose the GRR3 nucleotide and amino acid sequences in Figs. 15A and 17A. However, neither of the GRR3 sequences (nor Example 11, Fig. 15A, or Fig. 17A) is present in any of the three Fox I/Fox II priority applications listed above. As a result, no Fox priority application that pre-dates May 7, 1997 (the priority date of the pending claims acknowledged in the Office Action) discloses the sequences that were used as the bases of the present rejections. Because of this deficiency, the Fox I/Fox II disclosure cited in the present rejections does not constitute prior art under 35 USC § 102(e) and Fox I and Fox II therefore do not anticipate any of the pending claims.

In view of the foregoing remarks, applicants respectfully request that the Examiner withdraw the rejections of claims 1, 2, and 6-10.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is requested.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 13751-045003.

Respectfully submitted,

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Jack Brennan
Reg. No. 47,443

Fish & Richardson P.C.
Citigroup Center
52nd Floor
153 East 53rd Street
New York, New York 10022-4611
Telephone: (212) 765-5070
Facsimile: (212) 258-2291